

REPLACEMENT SHEET

Title: IL-15 ANTAGONISTS

Applicant(s): Dreher et al.

Filing Date: April 12, 2005 Serial No.: 10/530,987

Customer No.: 21559

Figure 1 a:

Amino acid sequence WT-IL-15-hIgG1:

NWVNVISDLKKTEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLLELQVISLESG  
DASIHDTVENLIILANNSLSSNGNVTESGCKECELEEKNIKEFLQSFVHIVQMF  
INTSDPKSADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV  
SHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKC  
KVSNAKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSD  
IAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVSMHEA  
LHNHYTQKSLSLSPGK

(SEQ ID NO: 4)

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Figure 1 b:

Amino acid sequence WT-IL-15-mIgG2a:

NWVNVISDLKKTEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLELQVISLESG  
DASIHDTVENLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMF  
INTSDPRGPTIKPCPPCKCPAPNLLGGPSVFIFPPKIKDVLMSLSPIVTCVVVD  
VSEDDPDVQISWVNNVEVHTAQTQTHREDYNSTLRVVSALPIQHQDWMSGKEFK  
CKVNNKDLPAPIERTISKPKGSVRAPQVYVLPPEEEMTKKQVTLTCMVTDFMPE  
DIYVEWTNNGKTELNYKNTEPVLDSDGSYFMYSKLRVEKKNWVERNSYSCSVVHE  
GLHNHHTTKSFSRTPGK

(SEQ ID NO: 5)

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Figure 2 a:

Amino acid sequence WT-IL-15:

NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLLELQVISLESG

DASIHDTVENLIILANNSLSSNGNVTESGCKECELEEKNIKEFLQSFVHIVQMF

INTS

(SEQ ID NO: 1)

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Figure 2 b:

Amino acid sequence hIgG1:

PKSADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP  
EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK  
ALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEW  
ESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSFSVMHEALHNHY  
TQKSLSLSPGK

(SEQ ID NO: 2)

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Figure 2 c:

Amino acid sequence mIgG2a:

PRGPTIKPCPPCKCPAPNLLGGPSVFIFPPKIKDVLMI SLSPIVTCVVVDVSEDD  
PDVQISWFVNNVEVHTAQTQTHREDYNSTLRVVSALPIQHQDWMSGKEFKCKVNN  
KDLPAPIERTISKPKGSVRAPQVYVLPPEEEMTKKQVTLTCMVTD FMPEDIYVE  
WTNNGKTELNYKNTEPVLDSDGSYFMYSKLRVEKKNWVERN SYSCSVVHEGLHNH  
HTTKSFSRTPGK

(SEQ ID NO: 3)

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Figure 3 a:

Amino acid sequence Igk8

NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLLELQVISLESG  
DASIHDTVENLIILANNSLSNNGNVTESGCKECEELEEKNIKEFLDSFVHIVDMF  
INTSDPRGPTIKPCPPCKCPAPNLLGGPSVFIFFPKIKDVLMLSLSPIVTCVVVD  
VSEDDPDVQISWVNNVEVHTAQQTQTHREDYNSTLRVVSALPIQHQDWMSGKEFK  
CKVNNKDLPAPIERTISKPKGSVRAPQVYVLPPEEEMTKKQVTLTCMVTDPMPE  
DIYVEWTNNGKTELNYKNTEPVLDSDGSYFMYSKLRVEKKNWVERNSYSCSVVHE  
GLHNHHTTKSFSRTPGK

(SEQ ID NO: 24)

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Figure 3 b:

Amino acid sequence 149-Fc

NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLLELQVISLESG  
DASIHDTVENLIILANNSLSSNGNVTESGCKECELEEKNIKEFLDSFVHIVQMF  
INTSDPRGPTIKPCPPCKCPAPNLLGGPSVFIFPPKIKDVLMSLSPIVTCVVVD  
VSEDDPDVQISWVNNVEVHTAQQTQTHREDYNSTLRVVSALPIQHQDWMSGKEFK  
CKVNNKDLPAPIERTISKPKGSVRAPQVYVLPPEEEMTKKQVTLTCMVTDFMPE  
DIYVEWTNNGKTELNYKNTEPVLDSDGSYFMYSKLRVEKKNWVERNSYSCSVVHE  
GLHNHHTTKSFSRTPGK

(SEQ ID NO: 25)

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Figure 4:

Nucleic acid sequence WT-IL-15-hIgG1:

AACTGGGTGAATGTAATAAGTGATTTGAAAAAACCGAAGATCTTATTCAATCTA  
TGCATATTGATGCTACTTTATATACGGAAAGTGATGTTACCCCCAGTTGCAAAGT  
AACAGCAATGAAGTGCTTTCTCTTGAGATTACAAGTTATTTCACTTGAGTCCGGA  
GATGCAAGTATTCATGATACAGTAGAAAATCTGATCATCCTAGCAAACAACAGTT  
TGTCTTCTAATGGGAATGTAACAGAATCTGGATGCAAAGAATGTGAGGAACTGGA  
GGAAAAAATATTAAAGAATTTTTCAGAGTTTGTACATATTGTCCAAATGTTT  
ATCAACACTTCGGATCCCAAATCTGCTGACAAAACCTCACACATGCCCCACCGTGCC  
CAGCACCTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCAAACCCAA  
GGACACCCCTCATGATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGGTGGACGTG  
AGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGAGGTGC  
ATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGT  
CAGCGTCTCACCCTGCTGACCAAGGACTGGCTGAATGGCAAGGAGTACAAGTGC  
AAGGTCTCCAACAAAGCCCTCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCA  
AAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCT  
GACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGAC  
ATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACCTACAAGACCACGC  
CTCCCGTGCTGGACTCCGACGGCTCCTTCTTCTCTACAGCAAGCTCACCGTGGA  
CAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCT  
CTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTAAATGATCTA  
GA

(SEQ ID NO: 9)



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Figure 5:

Nucleic acid sequence WT-IL-15-mIgG2a:

AACTGGGTGAATGTAATAAGTGATTTGAAAAAATTGAAGATCTTATTCAATCTA  
TGCATATTGATGCTACTTTATATACGGAAAGTGATGTTACCCCCAGTTGCAAAGT  
AACAGCAATGAAGTGCTTTCTCTTGGAGTTACAAGTTATTTCACTTGAGTCCGGA  
GATGCAAGTATTCATGATACAGTAGAAAATCTGATCATCCTAGCAAACAACAGTT  
TGTCTTCTAATGGGAATGTAACAGAATCTGGATGCAAAGAATGTGAGGAACTGGA  
GGAAAAAATATTAAAGAATTTTTCAGAGTTTTGTACATATTGTC<sup>1</sup>CAAATGTTT  
ATCAACACTTCGGATCCCAGAGGGCCCAACAATCAAGCCCTGTCCTCCATGCAAAT  
GCCAGCACCTAACCTCTTGGGTGGACCATCCGTCTTCATCTTCCCTCCAAAGAT  
CAAGGATGTACTCATGATCTCCCTGAGCCCCATAGTCACATGTGTGGTGGTGGAT  
GTGAGCGAGGATGACCCAGATGTCCAGATCAGCTGGTTTGTGAACAACGTGGAAG  
TACACACAGCTCAGACACAAACCCATAGAGAGGATTACAACAGTACTCTCCGGGT  
GGTCAGTGCCCTCCCCATCCAGCACCAAGGACTGGATGAGTGGCAAGGAGTTCAAA  
TGCAAGGTCAACAACAAGACCTCCCAGCGCCCATCGAGAGAACCATCTCAAAAC  
CCAAAGGGTCAGTAAGAGCTCCACAGGTATATGTCTTGCCTCCACCAGAAGAAGA  
GATGACTAAGAAACAGGTCACTCTGACCTGCATGGTCACAGACTTCATGCCTGAA  
GACATTTACGTGGAGTGGACCAACAACGGGAAAACAGAGCTAAACTACAAGAACA  
CTGAACCAGTCCTGGACTCTGATGGTTCTTACTTCATGTACAGCAAGCTGAGAGT  
GGAAAAGAAGAACTGGGTGGAAAGAAATAGCTACTCCTGTTTCAGTGGTCCACGAG  
GGTCTGCACAATCACCACACGACTAAGAGCTTCTCCCGGACTCCGGGTAAATGAG

(SEQ ID NO: 10)

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Figure 6 a:

Nucleic acid sequence WT-IL-15:

AACTGGGTGAATGTAATAAGTGATTTGAAAAAATTGAAGATCTTATTCAATCTA  
TGCATATTGATGCTACTTTATATACGGAAAGTGATGTTACCCCAGTTGCAAAGT  
AACAGCAATGAAGTGCTTCTCTTGGAGTTACAAGTTATTTCACTTGAGTCCGGA  
GATGCAAGTATTCATGATACAGTAGAAAATCTGATCATCCTAGCAAACAACAGTT  
TGTCTTCTAATGGGAATGTAACAGAATCTGGATGCAAAGAATGTGAGGAAGTGA  
GGAAAAAATATTAAAGAATTTTGCAGAGTTTGTACATATTGTCCAAATGTTC  
ATCAACACTTC

(SEQ ID NO: 6)

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Figure 6 b:

Nucleic acid sequence hIgG1:

CCCAAATCTGCTGACAAACTCACACATGCCCACCGTGCCCAGCACCTGAACTCC  
TGGGGGGACCGTCAGTCTTCCTCTTCCCCCAAACCCAAGGACACCCTCATGAT  
CTCCCGGACCCCTGAGGTCACGTGCGTGGTGGTGGACGTGAGCCACGAAGACCCT  
GAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAA  
AGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGT  
CCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAA  
GCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAG  
AACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGT  
CAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGG  
GAGAGCAATGGGCAGCCGGAGAACAACACTACAAGACCACGCCTCCCGTGCTGGACT  
CCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCA  
GCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTAC  
ACGCAGAAGAGCCTCTCCCTGTCTCCGGGTAAATGAT

(SEQ ID NO: 7)

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Figure 7:

Nucleic acid sequence mIgG2a:

CCCAGAGGGCCCACAATCAAGCCCTGTCTCCATGCAAATGCCCAGCACCTAACC  
TCTTGGGTGGACCATCCGTCTTCATCTTCCCTCCAAAGATCAAGGATGTACTCAT  
GATCTCCCTGAGCCCCATAGTCACATGTGTGGTGGTGGATGTGAGCGAGGATGAC  
CCAGATGTCCAGATCAGCTGGTTTGTGAACAACGTGGAAGTACACACAGCTCAGA  
CACAAACCCATAGAGAGGATTACAACAGTACTCTCCGGGTGGTCAGTGCCCTCCC  
CATCCAGCACCAGGACTGGATGAGTGGCAAGGAGTTCAAATGCAAGGTCAACAAC  
AAAGACCTCCCAGCGCCCATCGAGAGAACCATCTCAAACCCAAAGGGTCAGTAA  
GAGCTCCACAGGTATATGTCTTGCCTCCACCAGAAGAAGAGATGACTAAGAAACA  
GGTCACTCTGACCTGCATGGTCACAGACTTCATGCCTGAAGACATTTACGTGGAG  
TGGACCAACAACGGGAAAACAGAGCTAAACTACAAGAACACTGAACCAGTCCTGG  
ACTCTGATGGTTCTTACTTCATGTACAGCAAGCTGAGAGTGGAAAAGAAGAACTG  
GGTGGAAAAGAAATAGCTACTCCTGTTCAGTGGTCCACGAGGGTCTGCACAATCAC  
CACACGACTAAGAGCTTCTCCCGGACTCCGGGTAAATGAG

(SEQ ID NO: 8)

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Figure 8 a:

Nucleic acid sequence of murine IgK leader:

ATGGAGACAGACACACTCCTGCTATGGGTACTGCTGCTCTGGGTTCCAGGTTCCA  
CTGGTGAC

(SEQ ID NO: 11)

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Figure 8 b:

Nucleic acid sequence of human CD5 leader:

ATGCCCATGGGGTCTCTGCAACCGCTGGCCACCTTGTACCTGCTGGGGATGCTGG

TCGCTTCCTGCCTCGGA

(SEQ ID NO: 12)

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Figure 8 c:

Nucleic acid sequence of human CD4 leader:

ATGAACCGGGGAGTCCCTTTTAGGCACTTGCTTCTGGTGCTGCAACTGGCGCTCC  
TCCCAGCAGCCACTCAGGGA

(SEQ ID NO: 13)

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Figure 8 d:

Nucleic acid sequence of human IL-2 leader:

ATGTACAGGATGCAACTCCTGTCTTGCATTGCACTAAGTCTTGCACTTGTCACAA  
ACAGT

(SEQ ID NO: 14)



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Figure 9 a:

Nucleic acid sequence of human MCP leader:

ATGAAAGTCTCTGCCGCCCTTCTGTGCCTGCTGCTCATAGCAGCCACCTTCATTC  
CCCAAGGGCTCGCT

(SEQ ID NO: 15)

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Figure 9 b:

Nucleic acid sequence of the short native human IL-15 leader:

ATGTCTTCATTTTGGGCTGTTTCAGTGCAGGGCTTCCTAA

(SEQ ID NO: 16)

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Figure 9 c:

Nucleic acid sequence of the long native human IL-15 leader:

ATGAGAATTTGAAACCACATTTGAGAAGTATTTCCATCCAGTGCTACTTGTGTT  
TACTTCTAAACAGTCATTTTCTAACTGAAGCTGGCATTTCATGTCCTTCATTTTGGG  
CTGTTTCAGTGCAGGGCTTCCTAAACAGAAGCC

(SEQ ID NO: 17)

Figure 10:  
Igk8 nucleic acid sequence

ATGGAGACAGACACACTCCTGCTATGGGTACTGCTGCTCTGGGTTCAGGTTCCA  
CTGGTGACAACTGGGTGAATGTAATAAGTGATTTGAAAAAATTGAAGATCTTAT  
TCAATCTATGCATATTGATGCTACTTTATATACGGAAAGTGATGTTACCCCCAGT  
TGCAAAGTAACAGCAATGAAGTGCTTTCTCTTGGAGTTACAAGTTATTTCACTTG  
AGTCCGGAGATGCAAGTATTCATGATACAGTAGAAAATCTGATCATCCTAGCAAA  
CAACAGTTTGTCTTCTAATGGGAATGTAACAGAATCTGGATGCAAAGAATGTGAG  
GAACTGGAGGAAAAAATATTAAAGAATTTTGGACAGTTTGTACATATTGTGCG  
ACATGTTTCATCAACACTTCGGATCCCAGAGGGCCCAATCAAGCCCTGTCCTCC  
ATGCAAATGCCCAGCACCTAACCTCTTGGGTGGACCATCCGTCTTCATCTTCCCT  
CCAAAGATCAAGGATGTACTCATGATCTCCCTGAGCCCCATAGTCACATGTGTGG  
TGGTGGATGTGAGCGAGGATGACCCAGATGTCCAGATCAGCTGGTTTGTGAACAA  
CGTGGAAGTACACACAGCTCAGACACAAACCCATAGAGAGGATTACAACAGTACT  
CTCCGGGTGGTCAGTGCCCTCCCCATCCAGCACCAAGGACTGGATGAGTGGCAAGG  
AGTTCAAATGCAAGGTCAACAACAAAGACCTCCCAGCGCCCATCGAGAGAACCAT  
CTCAAACCCAAAGGGTCAGTAAGAGCTCCACAGGTATATGTCTTGCCTCCACCA  
GAAGAAGAGATGACTAAGAAACAGGTCCTGACCTGCATGGTCACAGACTTCA  
TGCCTGAAGACATTTACGTGGAGTGGACCAACAACGGGAAAACAGAGCTAAACTA  
CAAGAACACTGAACCAGTCCTGGACTCTGATGGTTCTTACTTCATGTACAGCAAG  
CTGAGAGTGGAAGAAGAACTGGGTGGAAAGAAATAGCTACTCCTGTTTCAGTGG  
TCCACGAGGGTCTGCACAATCACCACACGACTAAGAGCTTCTCCCGGACTCCGGG  
TAAATGAG

(SEQ ID NO: 26)

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Figure 11:

149-Fc nucleic acid sequence

ATGGAGACAGACACACTCCTGCTATGGGTACTGCTGCTCTGGGTTCAGGTTCCA  
CTGGTGACAACCTGGGTGAATGTAATAAGTGATTTGAAAAAATTGAAGATCTTAT  
TCAATCTATGCATATTGATGCTACTTTATATACGGAAAGTGATGTTACCCCCAGT  
TGCAAAGTAACAGCAATGAAGTGCTTTCTCTTGGAGTTACAAGTTATTTCACTTG  
AGTCCGGAGATGCAAGTATTCATGATACAGTAGAAAATCTGATCATCCTAGCAAA  
CAACAGTTTGTCTTCTAATGGGAATGTAACAGAATCTGGATGCAAAGAATGTGAG  
GAACTGGAGGAAAAAATATTTAAAGAATTTTTGGACAGTTTTGTACATATTGTCC  
AAATGTTTCATCAACACTTCGGATCCCAGAGGGCCCAATCAAGCCCTGTCTCC  
ATGCAAATGCCCAGCACCTAACCTCTTGGGTGGACCATCCGTCTTCATCTTCCCT  
CCAAAGATCAAGGATGTACTCATGATCTCCCTGAGCCCCATAGTCACATGTGTGG  
TGGTGGATGTGAGCGAGGATGACCCAGATGTCCAGATCAGCTGGTTTGTGAACAA  
CGTGGAAGTACACACAGCTCAGACACAAACCCATAGAGAGGATTACAACAGTACT  
CTCCGGGTGGTCAGTGCCCTCCCCATCCAGCACCAGGACTGGATGAGTGGCAAGG  
AGTTCAAATGCAAGGTCAACAACAAAGACCTCCCAGCGCCCATCGAGAGAACCAT  
CTCAAAACCCAAAGGGTCAGTAAGAGCTCCACAGGTATATGTCTTGCCTCCACCA  
GAAGAAGAGATGACTAAGAAACAGGTCACTCTGACCTGCATGGTCACAGACTTCA  
TGCCTGAAGACATTTACGTGGAGTGGACCAACAACGGGAAAACAGAGCTAAACTA  
CAAGAACTGAACCAGTCCTGGACTCTGATGGTTCTTACTTCATGTACAGCAAG  
CTGAGAGTGGAAAAGAAGAACTGGGTGGAAAGAAATAGCTACTCCTGTTCAAGTGG  
TCCACGAGGGTCTGCACAATCACCACACGACTAAGAGCTTCTCCCGGACTCCGGG  
TAAATGAG

(SEQ ID NO: 27)